DETAILED ACTION

This supplemental is in response to applicant's request for correction of typographical errors made in notice of allowability including claim 56, which is canceled and typographical errors made in the courtesy copy of allowed claims, 49 and 61 including "A" before "The". Corrections have been made to the action.

1. The appeal brief filed on 1/18/08 is entered.

Status of Claims

2, Claims 1,10,11,15,25, 29-32 and 35-69 are pending.

Claims 1, 10, 11, 15, 25, 29 , 30-32, 35-45, 63 and 66-69 are under examination.

Claims 46-62, 64 and 65 are withdrawn from consideration as drawn to a non elected invention.

Examiner's amendment

3. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Leana Levin on 4/11/08. The application has been amended as follows:

Claims 35 and 56 are canceled.

Claim 1. A culture comprising a culture medium and a bacterium responsible for Whipple's disease, said bacterium being isolated and established in culture <u>in a cell</u> such that the bacterium can reproducibly and detectably multiply over time in the culture medium for at least 72 days as detected by inverted microscopy, wherein the bacterium is *Tropheryma whippelii*.

Claim 11. A method for the in vitro diagnosis of diseases associated with infections caused by Tropheryma whippelii, comprising contacting serum or any other biological fluid of a patient

with ~~a~~ the culture according to claim 1 or a *Tropheryma whippelii* bacterium obtained from said culture, and detecting an immunological reaction.

Claim 29. ~~A~~ The method for the in vitro serological diagnosis according to claim 25, comprising:

- depositing a solution containing said antigen in or on a solid support;
- introducing serum or any other biological fluid into or onto said support;
- introducing a solution of a labeled antibody specific for a human immunoglobulin, which recognizes said antigen, into or onto the support;
- observing an incubation period;
-rinsing the solid support; and
-detecting an immunological reaction.

Claim 30. ~~A~~ The culture according to claim 1, wherein said culture is not a cell culture in monocyte cells.

Claim 31. ~~A~~ The culture according to claim 1, wherein said culture is a cell culture in immortalized cells other than monocyte cells.

Claim 32. ~~A~~ The culture according to claim 31, wherein the immortalized cells are fibroblast cells.

Claim 36. ~~A~~ The culture according to claim ~~35~~ 1 , wherein the cell has a dividing time greater than the doubling time of the bacterium.

Claim 37. ~~A~~ The culture according to claim 36, wherein the cell is a fibroblast cell.

Claim 38. ~~A~~ The culture according to claim 1, wherein the bacterium is capable of reproducibly and detectably multiplying over time in said culture medium through successive subcultures.

Claim 39. ~~A~~ The culture according to claim 1, wherein the bacterium has been established in culture through successive subcultures.

Claim 40. ~~A~~ The culture according to claim 1, wherein the bacterium is of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 41. ~~A~~ The culture according to claim 1, wherein the bacterium comprises a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5.

Claim 42. ~~A~~ The culture according to claim 41, wherein said culture medium does not comprise monocyte cells.

Claim 43. ~~A~~ The culture according to claim 42, wherein the bacterium is of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 44. ~~A~~ The culture according to claim 43, wherein the bacterium is in a cell having a dividing time greater than the doubling time of the bacterium, and the cell is in the culture medium.

Claim 45. ~~A~~ The culture according to claim 44, wherein the cell is a fibroblast cell.

Claim 46. A process of culturing *Tropheryma whippelii* bacteria responsible for Whipple's disease, comprising isolating and establishing said bacteria in cells in a culture medium such that said bacteria are capable of reproducibly and detectably multiplying over time in the culture medium for at least 72 days as detected by inverted microscopy.

Claim 47. ~~A~~ The process according to claim 46, wherein said bacteria have a doubling time of 18 days and are in cells having a dividing time greater than 18 days, and the cells are in the culture medium.

Claim 48. ~~A~~ The process according to claim 46, wherein said bacteria are in cells in the culture medium.

Claim 49. ~~A~~ The A process according to claim 48, wherein said cells have a dividing time greater than the doubling time of said bacteria.

Claim 50. ~~A~~ The process according to claim 49, wherein said doubling time is 18 days.

Claim 51. ~~A~~ The process according to claim 48, wherein said cells are not monocyte cells.

Claim 52. ~~A~~ The process according to claim 48, wherein said cells are fibroblast cells.

Claim 53. ~~A~~ The process according to claim 46, wherein the establishing step comprises establishing said bacteria in said culture medium through successive subcultures.

Claim 54. ~~A~~ The process according to claim 46, wherein the bacteria comprise a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5.

Claim 55. ~~A~~ The process according to claim 46, wherein the bacteria are of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 57. ~~A~~ The process according to claim ~~56~~ 46, wherein said cells in the culture medium have a dividing time greater than the doubling time of said bacteria.

Claim 58. ~~A~~ The process according to claim 57, comprising establishing said bacteria in said culture medium through successive subcultures.

Claim 59. ~~A~~ The process according to claim 58, wherein the cells in the culture medium are fibroblast cells.

Claim 60. ~~A~~ The process according to claim 59, wherein the bacteria are of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 61. ~~A~~ The A process according to claim 46, wherein said culture does not comprise monocyte cells.

Claim 62. ~~A~~ The process according to claim 46, further comprising maintaining the bacteria in culture for at least 72 days.

Claim 63. A culture comprising a culture medium and a bacterium responsible for Whipple's disease, said bacterium being isolated and established in culture in a cell such that the bacterium can reproducibly and detectably multiply over time in the culture medium for at least 72 days through successive subcultures, as detected by inverted microscopy, wherein the bacterium is of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202, wherein the bacterium comprises a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5.

Claim 64. A process of culturing *Tropheryma whippelii* bacteria responsible for Whipple's disease, comprising isolating and establishing said bacteria in cells in a culture medium such that said bacteria are capable of reproducibly and detectably multiplying over time in the culture medium for at least 72 days through successive subcultures, as detected by inverted microscopy, wherein the bacteria comprise a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5, and wherein the bacteria are of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 65. ~~A~~ The process according to claim 64, further comprising maintaining the bacteria in culture for at least 72 days.

Claim 66. ~~A~~ The culture according to claim 1, wherein the bacterium is capable of reproducibly and detectibly multiplying over time in a culture medium comprising fibroblast cells.

Claim 67. ~~A~~ The A culture according to claim 1, wherein the bacterium can reproducibly and detectably multiply over time in the culture medium for 72 days.

4. In view of amendment to the claims and arguments along with Declarations of record , all the rejections of record are withdrawn.

Remarks

5. Claims are drawn to a novel established culture that comprises a culture medium , cells and bacteria *Tropheryma whippelii* .

As the product is found allowable, withdrawn claims 46-62, 64 and 65 , drawn to a process of culturing *Tropheryma whippelii* have been rejoined . Therefore, the restriction requirement is withdrawn. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP 804.01.

6. Claims 1, 30-32, 36-45, 66, 67, 63, 68, 69, 46-62, 64, 65, 11, 15, 10, 25 and 29 are allowed and have been renumbered as 1-42 respectively.

Conclusion

7. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898.

/Padma v Baskar/
Examiner, Art Unit 1645

ALLOWED CLAIMS

Claim 1. A culture comprising a culture medium and a bacterium responsible for Whipple's disease, said bacterium being isolated and established in culture in a cell such that the bacterium can reproducibly and detectably multiply over time in the culture medium for at least 72 days as detected by inverted microscopy, wherein the bacterium is *Tropheryma whippelii*.

Claim 10. An antigen isolated from the *Tropheryma whippelii* bacterium in the culture according to claim 1, wherein said antigen is a protein of 200 kD determined by polyacrylamide gel electrophoresis using the Western blotting technique, which reacts with a specific monoclonal antibody directed against the bacterium *Tropheryma whippelii* responsible for Whipple's disease or an antigen of said bacterium, said antibody being produced by a hybridoma deposited in the CNCM of the Institut Pasteur under the Deposit No. I-2411.

Claim 11. A method for the in vitro diagnosis of diseases associated with infections caused by Tropheryma whippelii, comprising contacting serum or any other biological fluid of a patient with ~~a~~ the culture according to claim 1 or a *Tropheryma whippelii* bacterium obtained from said culture, and detecting an immunological reaction.

Claim 15. The method for the in vitro diagnosis according to claim 11, comprising:

- depositing a solution containing said *Tropheryma whippelii* bacterium in or on a solid support;

-introducing serum or any other biological fluid into or onto said support;

- introducing a solution of a labeled antibody specific for a human immunoglobulin, which recognizes said bacterium, into or onto the support;

-observing an incubation period;

- rinsing the solid support; and

-detecting an immunological reaction.

Claim 25. The method for the in vitro diagnosis of diseases associated with infections caused by Tropheryma whippelii, comprising contacting serum or any other biological fluid of a patient with the antigen of claim 10, and detecting an immunological reaction.

Claim 29. The method for the in vitro serological diagnosis according to claim 25, comprising:

- depositing a solution containing said antigen in or on a solid support;
- introducing serum or any other biological fluid into or onto said support;
- introducing a solution of a labeled antibody specific for a human immunoglobulin, which recognizes said antigen, into or onto the support;
- observing an incubation period;
-rinsing the solid support; and
-detecting an immunological reaction.

Claim 30. The culture according to claim 1, wherein said culture is not a cell culture in monocyte cells.

Claim 31. The culture according to claim 1, wherein said culture is a cell culture in immortalized cells other than monocyte cells.

Claim 32. The culture according to claim 31, wherein the immortalized cells are fibroblast cells.

Claim 36. The culture according to claim ~~35~~ 1 , wherein the cell has a dividing time greater than the doubling time of the bacterium.

Claim 37. The culture according to claim 36, wherein the cell is a fibroblast cell.

Claim 38. The culture according to claim 1, wherein the bacterium is capable of reproducibly and detectably multiplying over time in said culture medium through successive subcultures.

Claim 39. The culture according to claim 1, wherein the bacterium has been established in culture through successive subcultures.

Claim 40. The culture according to claim 1, wherein the bacterium is of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 41. The culture according to claim 1, wherein the bacterium comprises a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5.

Claim 42. The culture according to claim 41, wherein said culture medium does not comprise monocyte cells.

Claim 43. The culture according to claim 42, wherein the bacterium is of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 44. The culture according to claim 43, wherein the bacterium is in a cell having a dividing time greater than the doubling time of the bacterium, and the cell is in the culture medium.

Claim 45. The culture according to claim 44, wherein the cell is a fibroblast cell.

Claim 46. A process of culturing *Tropheryma whippelii* bacteria responsible for Whipple's disease, comprising isolating and establishing said bacteria in cells in a culture medium such that said bacteria are capable of reproducibly and detectably multiplying over time in the culture medium for at least 72 days as detected by inverted microscopy.

Claim 47. The process according to claim 46, wherein said bacteria have a doubling time of 18 days and are in cells having a dividing time greater than 18 days, and the cells are in the culture medium.

Claim 48. The process according to claim 46, wherein said bacteria are in cells in the culture medium.

Claim 49. The process according to claim 48, wherein said cells have a dividing time greater than the doubling time of said bacteria.

Claim 50. The process according to claim 49, wherein said doubling time is 18 days.

Claim 51. The process according to claim 48, wherein said cells are not monocyte cells.

Claim 52. The process according to claim 48, wherein said cells are fibroblast cells.

Claim 53. The process according to claim 46, wherein the establishing step comprises establishing said bacteria in said culture medium through successive subcultures.

Claim 54. The process according to claim 46, wherein the bacteria comprise a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5.

Claim 55. The process according to claim 46, wherein the bacteria are of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 57. The process according to claim 46, wherein said cells in the culture medium have a dividing time greater than the doubling time of said bacteria.

Claim 58. The process according to claim 57, comprising establishing said bacteria in said culture medium through successive subcultures.

Claim 59. The process according to claim 58, wherein the cells in the culture medium are fibroblast cells.

Claim 60. The process according to claim 59, wherein the bacteria are of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 61. The process according to claim 46, wherein said culture does not comprise monocyte cells.

Claim 62. The process according to claim 46, further comprising maintaining the bacteria in culture for at least 72 days.

Claim 63. A culture comprising a culture medium and a bacterium responsible for Whipple's disease, said bacterium being isolated and established in culture in a cell such that the bacterium can reproducibly and detectably multiply over time in the culture medium for at least 72 days through successive subcultures, as detected by inverted microscopy, wherein the bacterium is of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202, wherein the bacterium comprises a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5.

Claim 64. A process of culturing *Tropheryma whippelii* bacteria responsible for Whipple's disease, comprising isolating and establishing said bacteria in cells in a culture medium such that said bacteria are capable of reproducibly and detectably multiplying over time in the culture medium for at least 72 days through successive subcultures, as detected by inverted microscopy, wherein the bacteria comprise a rpoB gene comprising a partial sequence amplifiable by primers of a sequence identical to SEQ ID NO:4 or 5, and wherein the bacteria are of the *Tropheryma whippelii* bacterium strain deposited in the CNCM of the Institut Pasteur under Deposit No. I-2202.

Claim 65. The process according to claim 64, further comprising maintaining the bacteria in culture for at least 72 days.

Claim 66. The culture according to claim 1, wherein the bacterium is capable of reproducibly and detectibly multiplying over time in a culture medium comprising fibroblast cells.

Claim 67. The A culture according to claim 1, wherein the bacterium can reproducibly and detectably multiply over time in the culture medium for 72 days.

Claim 68. A culture comprising a culture medium and a bacterium responsible for Whipple's disease, said bacterium being isolated and established in culture in a cell in the culture medium, wherein the bacterium is *Tropheryma whippelii*, and said cell has a dividing time greater than the doubling time of the bacterium.

Claim 69. A culture comprising a culture medium and a bacterium responsible for Whipple's disease, said bacterium being isolated and established in culture in a cell in the culture medium, wherein the bacterium is *Tropheryma whippelii*, and the cell is selected such that it does not multiply so rapidly relative to the growth of the bacterium as to cause a dilution effect of the bacterium.

/Shanon A. Foley/
Supervisory Patent Examiner, Art Unit 1645